WHEN AND HOW TO TREAT GLAUCOMA


Randomized trials evaluated the effects of medical, laser, and surgical intervention.

BY DEIDRE ST. PETER, MD, AND CARA CAPITENA YOUNG, MD

LONG-TERM IMPACT OF IMMEDIATE VERSUS DELAYED TREATMENT OF EARLY GLAUCOMA: RESULTS FROM THE EARLY MANIFEST GLAUCOMA TRIAL

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Industry support: None

ABSTRACT SUMMARY

The Early Manifest Glaucoma Trial (EMGT) enrolled 255 patients with newly detected, untreated glaucoma. These individuals were randomly assigned to receive either immediate treatment with topical betaxolol and argon laser trabeculoplasty or no treatment, provided that no disease progression was detected. Long-term observation of the patients with perimetry, visual acuity testing, and tonometry continued for up to 21 years.

Patients' visual impairment (VI) due to glaucoma (as defined by the World Health Organization), perimetric mean deviation (MD) and rate of progression, and visual acuity were analyzed. Long-term results showed that more eyes in the treated versus untreated group developed VI or blindness (12.1% vs 11.0% and 9.4% vs 6.1%, respectively), but the difference was not statistically significant. The incidence of VI in at least one eye was also higher in the treated group (19.5% vs 18.7%), but again, the difference was not statistically significant. The untreated group had a worse median MD and a higher rate of disease progression in the worse eye than the treated group did (-14.75 dB vs -12.85 dB and -0.74 vs -0.60 dB/y, respectively). The differences were not significant.

STUDY IN BRIEF

- Prospective 21-year follow-up of the Early Manifest Glaucoma Trial (EMGT) assessed whether there was a higher incidence of visual impairment or blindness in patients who received either immediate treatment with topical betaxolol and argon laser trabeculoplasty or no treatment. No statistically significant difference in blindness or visual impairment was found between the two groups, but there were small differences in outcomes and visual field mean deviation.

WHY IT MATTERS

Physicians and patients may experience stress or confusion over glaucoma diagnosis and the decision of when to initiate treatment. Other studies have analyzed the ramifications of delayed treatment, but only one has reported the long-term effects on visual function.[2-6] This follow-up of the EMGT provides insight into the potential effects of delayed treatment on patients' visual acuity, visual fields, and visual impairment by analyzing the long-term outcomes of treatment versus initial monitoring. Patients' visual function did not appear to be greatly affected by delaying diagnosis and therefore treatment.

DISCUSSION

What are the clinical implications of the EMGT?

The goal of this prospective randomized controlled trial was to determine if the delayed treatment—and transitively delayed diagnosis—of early glaucoma was associated with long-term detrimental visual effects. Compared to the untreated group, a slightly higher number of patients in the treated group developed VI or blindness in one or both eyes. Conversely, the untreated group experienced faster visual field progression and had worse (by -1.9 dB) median perimetric MD values despite better baseline MD. These differences were not significant.

The EMGT found little difference overall in serious visual penalties between patients who began treatment immediately and those who received no initial treatment. This suggests that delays in the diagnosis and treatment of glaucoma may not be associated with serious long-term visual repercussions, although there could be some consequences. It therefore may not be harmful for providers and patients to retest or reevaluate a diagnosis before initiating treatment for early glaucoma.

What are the EMGT's strengths and limitations?

Two of the study's strengths are the intention-to-treat analysis and the large number of patients (treated, n = 128; untreated, n = 123), although more than half of them died and 28 were lost

to follow-up. A third strength is that participating physicians were allowed to choose and change additional treatment for their patients if disease progression was observed during the study period, mimicking real-world clinical medicine.

A major limitation of the EMGT is its lack of demographic diversity. The study population was predominantly European, so the trial's results may not be widely applicable. Furthermore, patients with advanced glaucoma were not included in the study, so its results should not be applied to this population.

STUDY IN BRIEF

- A prospective, randomized, multicenter noninferiority study compared the effectiveness and safety of the Xen Gel Stent (AbbVie) and trabeculectomy. The stent was found to be noninferior in achieving a 20% or greater IOP reduction at 12 months without an increase in medication, clinical hypotony, vision loss to counting fingers, or secondary surgical intervention.

WHY IT MATTERS

Trabeculectomy is the gold standard of glaucoma filtering surgery but can be associated with several complications.[8,9] Retrospective comparison studies have found that trabeculectomy is more effective than the gel stent at lowering IOP. Some studies have shown better safety with the gel stent, whereas others have found no difference between the two procedures.[10-12] This is the first prospective randomized trial to compare the two procedures, and it provides insight into the stent's place in surgeons' arsenals.

GEL STENT VERSUS TRABECULECTOMY: THE RANDOMIZED, MULTICENTER, GOLD-STANDARD PATHWAY STUDY (GPS) OF EFFECTIVENESS AND SAFETY AT 12 MONTHS

Sheybani A, Vera V, Grover DS, et al[7]
Industry support: None

ABSTRACT SUMMARY

The Gold-Standard Pathway Study (GPS) is a prospective, randomized, multicenter noninferiority study designed to compare the effectiveness and safety of a gel stent (Xen Gel Stent, AbbVie) versus trabeculectomy in patients (N = 115) with open-angle glaucoma receiving topical therapy. Patients were randomly assigned 2:1 to receive a gel stent (n = 77) or undergo trabeculectomy (n = 38). The primary endpoint of the study was the percentage of patients who achieved a 20% or greater reduction in IOP from baseline at 12 months without additional medication, clinical hypotony, vision loss, or secondary surgical intervention. Secondary outcomes were mean IOP, medication count, postoperative intervention rate, visual recovery, and patient-reported outcomes.

After 12 months, 62.1% and 68.2% of the gel stent and trabeculectomy patients, respectively, had achieved the primary endpoint (P = .487). Both groups achieved significant reductions in mean IOP and medication count, but the trabeculectomy group experienced a significantly greater IOP reduction. The gel stent group had fewer in-office postoperative interventions, a faster visual recovery, and greater 6-month improvements in visual function.

DISCUSSION

How did effectiveness and safety between treatment groups compare?

Most patients in both groups achieved the primary endpoint. The gel stent was found to be noninferior to trabeculectomy.

There was no significant difference in medication reduction or percentage of medication-free patients between groups. Among medication-free patients, IOP was significantly lower in the trabeculectomy group (P = .12). Unsurprisingly, a higher percentage of patients in that group required in-office procedures, of which laser suture lysis accounted for half. Importantly, seven patients in the gel stent arm and one patient in the trabeculectomy arm required secondary surgical intervention. Visual recovery at 12 months was significantly better in the gel stent group (P = .021).

Surveys were administered to assess patient-reported outcomes. Most of the surveys showed greater patient satisfaction with the gel stent. A work impairment questionnaire found significantly worse productivity for trabeculectomy patients at week 1 and month 3 but not at month 12.

What are the implications of the GPS for clinical practice?

Although the gel stent was found to be noninferior to trabeculectomy, the trabeculectomy group was more likely to have lower IOPs and require fewer medications. The gel stent group had faster visual recovery and higher patient satisfaction overall. More patients in the gel stent group required further surgical intervention than in the trabeculectomy group, but fewer of the patients in the gel stent group experienced clinical hypotony. Based on these results, the gel stent may be a good option for individuals who need a lower IOP and can tolerate IOP-lowering medications and additional surgery. Trabeculectomy may be a better alternative for someone who needs a very low IOP to prevent glaucomatous progression.

The observed differences in patients' postoperative experiences, visual recovery, and satisfaction may guide the choice of surgical procedure and preoperative counseling. ■

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1. Heijl A, Peters D, Bengtsson B. Long-term impact of immediate versus delayed treatment of early glaucoma: results from the Early Manifest Glaucoma Trial. *Am J Ophthalmol*. 2023;252:286-294.
2. Miglior S, Zeyen T, Pfeiffer N, Cunha-Vaz J, Torri V, Adamsons I; European Glaucoma Prevention Study (EGPS) Group. Results of the European Glaucoma Prevention Study. *Ophthalmology*. 2005;112(3):366-375.
3. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma Collaborative Normal-Tension Glaucoma Study Group. *Am J Ophthalmol*. 1998;126(4):498-505.
4. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M; Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol*. 2002;120(10):1268-1279.
5. Garway-Heath DF, Lascaratos G, Bunce C, Crabb DP, Russell RA, Shah A; United Kingdom Glaucoma Treatment Study Investigators. The United Kingdom Glaucoma Treatment Study: a multicenter, randomized, placebo-controlled clinical trial: design and methodology. *Ophthalmology*. 2013;120(1):68-76.
6. Kass MA, Gordon MO, Gao F, et al; Ocular Hypertension Treatment Study Group. Delaying treatment of ocular hypertension: the Ocular Hypertension Treatment Study. *Arch Ophthalmol*. 2010;128(3):276-287.
7. Sheybani A, Vera V, Grover DS, et al. Gel stent versus trabeculectomy: the randomized, multicenter, Gold-Standard Pathway Study (GPS) of effectiveness and safety at 12 months. *Am J Ophthalmol*. 2023;252:306-325.
8. Gedde SJ, Herndon LW, Brandt JD, Budenz DL, Feuer WJ, Schiffman JC; Tube Versus Trabeculectomy Study Group. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol*. 2012;153(5):804-814.e1.
9. Wang W, Zhang X. Meta-analysis of randomized controlled trials comparing Ex-Press implantation with trabeculectomy for open-angle glaucoma. *PLoS One*. 2014;9(6):e100578.
10. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. *Ophthalmology*. 2017;124(11):1579-1588.
11. Cappelli F, Cutolo CA, Olivari S, et al. Trabeculectomy versus Xen gel implant for the treatment of open-angle glaucoma: a 3-year retrospective analysis. *BMJ Open Ophthalmol*. 2022;7(1):e000830.
12. Stoner AM, Capitena Young CE, SooHoo JR, et al. A comparison of clinical outcomes after Xen Gel Stent and Ex-Press glaucoma drainage device implantation. *J Glaucoma*. 2021;30(6):481-488.

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